REMARKS

Claims 1 and 2 have been amended. Claims 1-6 remain pending in the present application. Support for the amendments can be found in the specification and claims as filed. Accordingly, the amendments do not constitute the addition of new matter. Reconsideration of the application in view of the foregoing amendments and following comments is respectfully requested.

Rejection of Claims under 35 U.S.C. § 112, second paragraph

The Examiner rejected Claims 1-6 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner objected to the term "recombinant antigen or synthetic peptide in said sample" because she believes that recombinant antigens or synthetic peptides are generally not in patient samples.

As suggested by the Examiner, Claim 1 has been amended to recite "determining a level of antibodies in a saliva sample from said patient, wherein said antibodies are able to bind to an autoantigen or a corresponding recombinant antigen or synthetic peptide for cardiovascular disease."

The Examiner rejected Claim 2 because of the term "immune complexes." As amended, Claim 2 recites "C1q immune complexes." Support for the amendment can be found in Example 7 which utilizes C1q immune complexes.

Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejections under 35 U.S.C. § 112, second paragraph.

Rejection of Claims under 35 U.S.C. § 112, first paragraph

The Examiner rejected Claims 1-6 under 35 U.S.C. § 112, first paragraph, because she believes that the specification does not provide enablement for a method for prediction of early pathogenic reaction for a cardiovascular disease. The Examiner states that there is enablement for "a method for detecting antibodies against certain autoantigens and for indicating the presence or possibility of cardiovascular disease."

As amended, Claim 1 recites "a method for indicating presence or possibility of cardiovascular disease in a patient." Therefore, the claim is now commensurate in scope with the subject admitted to have been enabled by the Examiner.

The Examiner rejected Claims 1 and 3-6 under 35 U.S.C. § 112, first paragraph, because she believes that the specification does not provide enablement for a method for detecting antibodies against any and all autoantigens. However, Claim 1 does not recite any and all antigens. Rather, Claim 1 recites "antibodies [that] are able to bind to an autoantigen or a corresponding recombinant antigen or synthetic peptide associated with cardiovascular disease." (emphasis added)

According to M.P.E.P.2164.02, "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art...would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation."

One of ordinary skill in the art would be able to readily identify autoantigens for cardiovascular disease. A large number of representative examples of cardiovascular disease-associated autoantigens are disclosed in the specification and are recited in Claim 2. These include myosin, oxidized LDL, heat shock protein-60, β-2-glycoprotein-1, platelet glycoprotein, and C1q immune complexes. Furthermore, Paragraph [0003] of the specification states that "the American College of Cardiology has issued a list of harmful pathogens as possible links to heart disease." These harmful pathogens can include autoantigens. The specification further states, in paragraph [0004] that "[t]raditionally, it is assumed that infectious agents induce disease by direct tissue damage via secretion of toxins or different antigens, particularly myosin. These toxins may directly or indirectly induce tissue damage and cause release of tissue antigens." These toxins and antigens can be readily identified by one skilled in the art as autoantigens related to cardiovascular system or immunological system. Accordingly, the specification provides a broad enabling disclosure, such that those skilled in the art would be able to make and use the claimed invention without undue experimentation.

Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejections under 35 U.S.C. § 112, first paragraph.

Rejection of Claims under 35 U.S.C. § 103

The Examiner rejected Claims 1-6 under 35 U.S.C. § 103(a) as being unpatentable over Kovanen et al. in view of Stone et al. (*Journal of Human Stress*, 1987, Vol. 13, pp. 136-140).

Kovanen et al. discloses elevated levels of IgA, IgE, and IgG in patients with established arteriosclerosis and myocardial infarction or cardiac death. Kovanen et al. also discloses autoantigens and several exogenous antigens as having been implicated in the pathogenesis of myocardial infarction including oxidized LDL and cardiolipin.

Stone et al. discloses that "secretory IgA (s-IgA) is very different from serum immunoglobulin in that it is much larger and probably binds invading organisms more effectively than the form of IgA in serum. S-IgA can be collected rather simply and inexpensively in saliva and quantitated with a readily available assay, radial immunodiffusion (RID)."

According to M.P.E.P.2141.02, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention."

Kovanen does not disclose that levels of IgA, IgE, and IgG can be measured with saliva samples. While Stone et al. discloses that S-IgA can be collected rather simply and inexpensively in saliva, Stone et al. does not teach or suggest that there is a proportional relationship between serum and saliva IgA antibodies. Indeed, Stone et al. does not experiment with comparisons of serum and saliva IgA antibody levels. Moreover, in Stone et al, fluctuations of saliva IgA antibody levels can occur with mere stress. Accordingly, Stone et al. suggests that saliva IgA antibody levels indicates "immune system function or ability to protect from infection if the antigen were infectious," not "presence or possibility of cardiovascular disease," as recited in the present claims.

Externest et al., cited in the accompanying Information Disclosure Statement, is a reference published in 2000, and after the Stone et al. 1987 publication date. Accordingly, Externest et al. was published near the time of filing of the present application. Externest et al. discloses that there are conflicting reports about the usefulness of analysis of antibody immune status using easy-to-sample specimens, such as saliva and feces. (See page 3835, first column,

second paragraph.) These conflicting reports may be the result of a relationship of specific antibody responses at different effector sites being dependent on the type and dose of antigen. (See page 3835, second column, second paragraph.) The Externest reference concludes that any relationship between serum, saliva, or urine IgA levels as a predictor of other sIgA release has a "strong dependence on antigen type and dosage for these relationships." See Abstract. Thus, the uncertainty of the relationship between secretory and serum IgA, as taught in Externest et al., would not suggest to one of ordinary skill in the art that it would be advisable to combine Kovanen et al. and Stone et al. Therefore, there would not be a reasonable expectation of success of combining Kovanen et al. and Stone et al. to obtain the claimed invention in view of the more recent disclosure of Externest et al. Without such a reasonable expectation, no *prima facie* showing of obviousness can be established by the combination of Kovanen et al. and Stone et al.

Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 103(a).

CONCLUSION

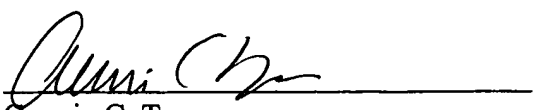
In view of the foregoing amendments and comments, it is respectfully submitted that the present application is fully in condition for allowance, and such action is earnestly solicited.

The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully requested to call the undersigned in order to resolve such issue promptly.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 20, 2004

By: 

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